

ISIS-4789

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

**In re application of:
Manoharan et al.**

Serial No.: Not Yet Assigned

Group Art Unit: Not Yet Assigned

Filed: Not Yet Assigned

Examiner: Not Yet Assigned

**For: OLIGONUCLEOTIDES HAVING A-DNA FORM AND B-DNA FORM
CONFORMATIONAL GEOMETRY**

**EXPRESS LABEL NO. EL650276764US
DATE OF DEPOSIT: October 4, 2001**

Assistant Commissioner for
Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Prior to examination of the above-captioned patent application, Applicants respectfully request entry of the following amendments, without prejudice:

In the Claims

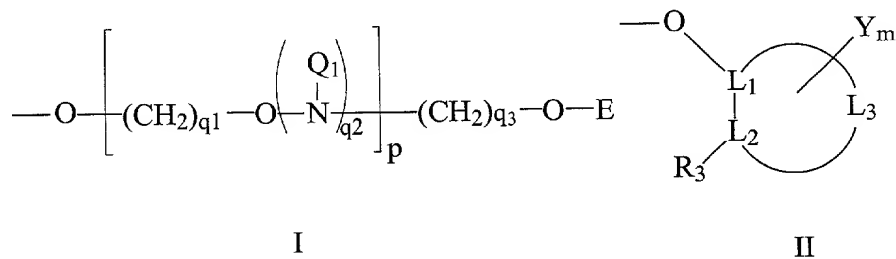
Please cancel claims 14-17, 19-20 and 33-36, without prejudice, and amend claims 1 and 4 as follows:

1. (Amended) An oligonucleotide comprising a plurality of nucleotides, wherein:

a first portion of said plurality of nucleotides have B-form conformational geometry and are joined together in a continuous sequence, at least two of said nucleotides of said first portion being ribonucleotides; and

a further portion of said plurality of nucleotides are ribonucleotide that have A-form conformation geometry and are joined together in at least one continuous sequence.

4 (Amended). The oligonucleotide of claim 1 wherein each nucleotide of said further portion, independently, is a 2'-fluoro nucleotide or a nucleotide having a 2'-substituent having the formula I or II:



wherein

E is C₁-C₁₀ alkyl, N(Q₁)(Q₂) or N=C(Q₁)(Q₂);

each Q₁ and Q₂ is, independently, H, C₁-C₁₀ alkyl, dialkylaminoalkyl, a nitrogen protecting group, a tethered or untethered conjugate group, a linker to a solid support, or Q₁ and Q₂, together, are joined in a nitrogen protecting group or a ring structure optionally containing at least one additional heteroatom selected from N and O;

R₃ is OX, SX, or N(X)₂;

each X is, independently, H, C₁-C₈ alkyl, C₁-C₈ haloalkyl, C(=NH)N(H)Z, C(=O)N(H)Z or OC(=O)N(H)Z;

Z is H or C₁-C₈ alkyl;

L₁, L₂ and L₃ form a ring system having from about 4 to about 7 carbon atoms or having from about 3 to about 6 carbon atoms and 1 or 2 heteroatoms selected from oxygen, nitrogen and sulfur and wherein said ring system is aliphatic, unsaturated aliphatic, aromatic, or saturated or unsaturated heterocyclic;